Recommendations of the Advisory Committee to the Director, CDC Concerning Laboratory Safety at the Food and Drug Administration July 17, 2015

In July 2014, CDC announced the formation of the External Laboratory Safety Workgroup (ELSW) of the Advisory Committee to the Director (ACD), Centers for Disease Control and Prevention. Although the ELSW was established as a workgroup of the ACD, CDC, HHS Secretary Burwell charged ELSW to review laboratory safety practices at the Food and Drug Administration (FDA) and the National Institutes of Health (NIH), in addition to CDC. As a workgroup of the ACD, the ELSW reports directly to the ACD. ELSW proposals are presented to the ACD, and, if adopted, they are provided to the CDC Director and then to the HHS Secretary. At the July 17, 2015, meeting of the ACD, the ELSW presented its observations and proposals regarding FDA's laboratory safety program. The ELSW met with FDA leadership and laboratory safety staff via teleconference since September 2014, and they had a four-day on-site meeting at FDA's facilities in Silver Spring and College Park, Maryland, in May 2015. The proposals were drawn from information gathered from these discussions in staff engagement sessions, in-person observations of laboratories, and a review of protocols, policies, and procedures related to laboratory safety at the agency. Below are the recommendations of the ACD, CDC, that were adopted at the July 2015 meeting.

ELSW Observations

The External Laboratory Safety Workgroup visited the White Oak, MD campus of the Food and Drug Administration (FDA), May 11-13, 2015. This site visit was conducted at the request of Secretary Burwell, Department of Health and Human Services, to examine and evaluate the organization of FDA laboratory and research safety programs in supporting scientific functions and to make proposed recommendations for improvements to these programs. The site visit was productive and well-organized. We thank Dr. Ostroff, Dr. Leiphart, Dr. DeGrasse, Mr. Matt Amann, Ms. Sarah Wiley, and Ms. Judith Talbot for their cooperation, diligent work and hospitality.

We present for consideration the following observations made during our visit concerning FDA laboratory safety programs and associated proposals for improvements to these safety programs.

Observation: Organizational Structure of the Safety Program at the FDA

The FDA is a complex organization which operates facilities and programs across the country. Organizationally, the FDA is structured as a collection of large Centers [e.g. Center for Biologics Evaluation and Research (CBER), Center for Devices and Radiological Health (CDRH), Center for Drugs Evaluation and Research (CDER), Center for Food Safety and Applied Nutrition (CFSAN), Center for Tobacco Products (CTP), Center for Veterinary Medicine (CVM), and National Center for Toxicological Research (NCTR)] each of which seems to operate primarily as an independent entity. In this environment, Centers have developed important aspects of the research safety program independently, with some safety programs more fully developed than others. Many of these programs are robust and

appear to work well and efforts to re-organize and improve lab safety should be careful to not compromise the quality of programs that are working well. It is clear that the Agency is at a critical juncture as it relocates to a new campus and embarks upon the development of new lab safety programs and infrastructure [e.g. Institutional Biosafety Committee (IBC)] as well as expansion of existing programs. The timing of the move to a new campus being coincidental with this safety program review presents a great opportunity for initiating programmatic improvements to laboratory and research safety.

Good laboratory safety programs usually employ aspects of a centralized program. This centralized approach promotes the establishment of institutional expectations in the realm of lab/research safety that are consistent across the Agency. Centralized programmatic elements provide opportunities for shared best practices and lessons learned. Finally, centralized programs provide economies of scale and can provide infrastructure (e.g. shared databases, IT elements) that promote visibility, efficiency and economical use of staff and other resources. However, good lab safety programs also contain elements of familiarity and specificity that are best delivered via LOCAL mechanisms and programs; these elements are essential to the mitigation of the REAL risks presented by SPECIFIC experimental elements and specific experimental activities encountered in each Center and even in each lab. In an entity with broadly diverse experimental activities, site-specific programmatic elements such as training and auditing also must be developed.

The ELSW observed that individuals at the FDA are demonstrably taking responsibility for laboratory safety and feel accountability to their home Center; this accountability should, however, extend to the Agency level. The major challenge for the FDA is, therefore, to establish a more robust centralized (headquarters) EH&S program while at the same time not losing or damaging local, Center and lab-specific, elements. The NIH Model where Central coordinated staff are deployed out to Centers works well, based upon the observations made by the ELSW earlier in 2015. This Central Office model, with deployed safety staff reporting to a central line of authority, would provide consistency yet retain the independence of the safety staff needed to minimize potential conflicts of interest.

ACD Recommendations:

1. An Agency-wide institutional vision for FDA lab/research safety programs needs to be more fully developed and the implementation of mechanisms for improvement must be strategic.
2. Agency leadership should focus on providing a common approach to the safety program and define desired outcomes. While safety challenges are varied across the Centers, as well as being specific to the labs within the Centers, institutional Agency-level leadership and oversight in the realm of laboratory safety is needed.
3. The Safety Officers should report to Institutional Headquarters rather than the Centers they oversee to avoid conflict-of-interest situations. In addition, the Responsible Official (RO) should be represented at the central Headquarters level and not be assigned at Center level as this also presents a potential conflict of interest. As the Select Agent Program grows, there cannot be more than one RO for a given site.

4. This centralized model with deployed staff presents fiscal implications, in that funding for safety initiatives, programs and personnel should be derived from a Central budget.

Observation: Laboratory Safety Leadership
We are encouraged by the plan to elevate the status of the laboratory safety leadership within the FDA hierarchy.

ACD Recommendations:
1. The responsibilities and authorities of this function must be strategic and need to be more fully developed and carefully considered, as well as the reporting structure, e.g. Office of the Commissioner or the Office of the Chief Scientist.
2. Funding for this function should not be drawn from Center's budgets but rather from a central source. It is important that the Centers fully "buy-in" to the need for laboratory safety leadership. If the Center's budget is reduced to support the function, resentment may result and this will defeat the purpose for its establishment.
3. In addition, the roles & responsibilities of headquarters Environmental Health and Safety (EH&S) going forward, including lines of authority, particularly in the context of the proposed new leadership model, should be better defined.
4. While it is commendable that the FDA has considered and understood the approach of the CDC to establish a laboratory safety leadership position, it is important to remember that these Agencies' missions are varied and different and that what may be the right approach for CDC is not necessarily the right approach for the FDA. What is important is that this leader must be cognizant of the health and safety status of staff and must have the ability to report directly to the Commissioner on these matters in a timely way.

Observation: Long term role of the LSPPW
The discovery of the smallpox vials was well handled as were the follow-up actions taken. Most importantly, this incident demonstrated that FDA staff feels empowered to report incidents in spite of their potential negative impact and that leadership responded responsibly and promptly. In particular, the work of the Internal Lab Safety Working Group (LSPPW) has been laudable. The commitment and leadership of Kristine Leiphart, Jeff DeGrasse and Matt Amann is quite evident on these issues.

ACD Recommendations:
1. The LSPPW, chartered by the Commissioner, has performed its task extremely well and should continue moving forward as part of the institutional safety structure. They are a good leadership team and are clearly committed to seeing this process through, even though it is not there yet. The LSPPW should be continued and charged with the development of specific goals supporting the missions of the FDA.
2. Center level safety committees with represented membership on a Central *Uber* Safety Committee, with links to the IBC and IACUC, would be helpful. The LSPPW could play the role of the Central Uber Safety Committee; laboratory safety leadership could serve to chair this uber committee.

Observation: Inventory System
New efforts to link safety competencies and compliance to a performance evaluation program (e.g. as they are doing in the Hazardous Biological Agents and Toxins (HBAT) program) are excellent. New plans for inventory management in HBAT program are also commendable. If they work as planned, they may be a model for other institutions. We were concerned, however, by some reports that not all components of the wide-spread FDA enterprise were committed to using a single electronic format for record keeping and monitoring of inventories.

ACD Recommendations:
1. The LSPPW should be charged with the implementation of the inventory system and auditing to assure that the system is maintained and updated to meet the need of the agency.
2. A single electronic system should be employed throughout FDA for this purpose.

Observation: Institutional Biosafety Committee
The FDA created an independent Institutional Biosafety Committee (IBC) in 2013. We applaud this effort and the commitment to implement the important risk assessment and risk mitigation activity at an institutional level via the IBC. The IBC membership is dedicated and takes their job very seriously; we applaud their effort. Similarly, we believe that the plan to consolidate IACUC is also a laudable effort. Our experience is that these institutional level committees provide consistency of risk assessments and safety expectations supporting FDA missions and promotes Agency-wide communication around research safety.

ACD Recommendations:
1. We believe that cross-representation across the IBC and IACUC should be considered.
2. As the NIH has done, we recommend that questions and discussion concerning *Dual-use Research of Concern* be incorporated into the PI's standard Risk assessment and IBC application for approval. The IBC Risk Assessment tool (*IBC Application*) could also be improved to elicit more information critical to the risk assessment process.
3. The FDA should monitor the pace of the IBC reviews. We acknowledge that the IBC has had a huge workload because of the transition to the White Oak campus, however, we heard that some PIs are frustrated by the pace of the process. If the pace does not improve in next few months, the FDA should consider adding people to the group to help speed things up. Another possibility is to consider providing incentives (financial or leave, etc.) for the IBC to work more hours to get things moving through the system.
4. We believe that efficiencies can be improved in the IBC review process by devoting more resources for PRE-REVIEW by biosafety officers and that processes for expedited review be considered.

Observation: Occupational Health
There is not a clear view in the Centers of what staff should expect from Occupational Health. In addition, Occupational Health services available to ORISE Fellows do not seem to be equivalent to those available to Federal employees.

ACD Recommendations:

1. Clarify to employees what the Occupational Health Office does (and does not do). The central EH&S office should support the proposed development of databases that will track immunization, vaccine compliance etc.
2. ORISE Fellows and Federal employees who work in laboratories should have equivalent Occupational Health and Safety services as do Federal employees.
3. Develop post-exposure follow-up procedures to be consistent throughout the institution and not Center-oriented.

Observation: Training

Multiple approaches to safety training have been developed, including on-line training and lab-specific training, but this effort is not standardized across the FDA. There seems to be ambiguity in the role of the FDA university versus the Centers in designing and delivering training.

ACD Recommendations:

1. We recommend that the headquarters EH&S survey the Centers to find out where specific needs and gaps exist. For instance, we heard that, in one Center, staff did not seem to know procedures for whom to call in emergency medical situations. The needs for CBER as compared to CFSAN in terms of training, outreach, etc. are very different and it is likely that this is the case across the FDA.
2. There is a need for more granular information that focus groups can provide to understand the particular needs within the Center, as well as the baseline views of the scientists and employees there. It would also be valuable to have more concrete data assembled every year on accidents. How many accidents exactly have occurred in each Center, each year? What were the patterns? What steps have been taken to reduce them in the coming year. This information should be tracked over time to demonstrate progress. The NIH has a good model for tracking incidents.
3. We would encourage the FDA to report near-misses and disseminate lessons learned to other scientists as a way to continuously improve quality.
4. A modular training model would help address site-specific safety needs while establishing consistency in training effort and content. Additionally, it appears that at some sites important training is not mandatory and that competency assessments (post-tests) are not performed. In addition to written competency assessments, technical competency in the lab should be assessed and documented.
5. Responsibilities for training should be clarified between the centers and the FDA university.

Observation: Communication

We learned from leadership about many initiatives that are underway to improve lab safety programs; however, we also heard that staff are not aware of many of these initiatives. We believe that efforts to communicate these initiatives, their rationale and criticality to the FDA community can be improved. Specifically, the role of the Occupational Health Program and the availability of this program to FDA staff as well as contractor employees is not well understood by the FDA staff. More specifically, the feedback from CBER staff was different from CFSAN staff, perhaps reflecting the different safety cultures of the two Centers. In

particular, the CBER group felt that the Safety Program they have works well for them and they are reluctant to see the safety function move to a "headquarters" office, not wanting to "break" a process that was working for them. CFSAN staff, in contrast, indicated a need for a stronger biosafety presence at CFSAN and felt they would benefit from more electronic training as well as more actual hands-on interactive training

ACD Recommendations:

1. Increase the visibility of signs and phone numbers that people can use to call with any safety concerns. The FDA need ways for those who feel least empowered to easily call with concerns.
2. Improve communication around the Occupational Medicine Program. A sentiment that this program was reactive rather than proactive was also articulated.
3. Develop an institution-wide communication program that emphasizes the FDA-way of doing good science safely.